REMARKS

Reconsideration of this application is requested. Claims 16-38 will be active in the application upon entry of this Amendment.

The original 15 claims in the application are replaced with a new claim set of 23 claims in which claims 16-29 are directed to a composition and claims 30-38 are directed to a process related to that composition. To form the new claims set, original claims 2, 5, 6, and 7 have been deleted; original claim 3 has been divided into three dependent claims; and original claim 1 has been amended in order to more particularly point out and distinctly claim the invention and now appears as new claim 16. Attached for the examiner's convenience is the text of the new claims in which relevant additions to previous claim language are underlined and relevant deletions are in square brackets. Reference is also made to locations in the specification from which the additions to the claim language drawn form the original claim set find origin. The language in the process claims finds origin in the respective relevant composition claims.

With respect to the election of the single disclosed species required in the office action related to the original claim set, the following are identified:

A specific non-aqueous medium is: ethyl oleate.

A specific surfactant system is: a phospholipid.

A specific hydrophilic substance is: ethanol.

An examination on the merits ins awaited taking into account the Information Disclosure Statements filed February 2, 2000 and April 23, 2001.

Respectfully submitted,

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1. A composition comprising stable solid (see page 11, line 8) particles of a [surface modified] water-insoluble biologically active substance of a [mean size] volume weighted mean particle size (see page 15, lines 23-24) in the range of 0.01 to 10 micrometers, which particles are dispersed in a non-aqueous carrier system comprised of:

(a) a non-aqueous hydrophobic liquid (see page 17, line 29) [medium] in which [the]said biologically active substance is not soluble or is poorly soluble; and

(b) a surfactant system consisting of at least one surfactant which is soluble in [the]said non-aqueous hydrophobic liquid (see page 17, line 29) [medium], wherein [and] at least a portion of (see page 16, lines 24-45) which surfactant system absorbs to the surface of [the]said particles [biologically active substance]; and

(c) [optionally] a quantity of not more than about 10% of the total weight of said composition of one or more hydrophilic substance that provides a self-dispersing property to said composition[.],

wherein [said composition self-disperse] upon addition of said composition to a[n] fluid (see page 15, line 30) aqueous medium, said composition self-disperses in said fluid aqueous medium (see page 15, line 30) to form a suspension comprising [components of] droplets (see page 16, line 1) of non aqueous hydrophobic liquid (see page 17, line 29) [medium carrier system] containing particles of surface stabilized water-insoluble biological substance suspended in the oily droplets of the dispersion (see page 23, lines 24-26) and [stable] particles of said water-insoluble biologically active substance migrated into said fluid aqueous medium (see page 16, line 9) wherein said particles have a size in the range of 0.01 to 10 micrometers and have associated therewith on the surface at least a portion of said surfactant system.

2. The composition[s] of claim 1 [and 2] where [the non-aqueous carrier system consists of: (a)] at least one component of the non-aqueous hydrophobic liquid

[medium component] is selected from the group consisting of an oil[s] derived from [vegetable or] animal origin[s]; a vegetable oil[s]; a fish oil[s]; a fish oil free fatty acid[s]; oleic acid; linoleic acid; a poly-unsaturated fatty acid[s]; [fatty acid esters; triglycerides;] caprilic/capric triglyceride; caprylic/capric/linoleic triglyceride; a synthetic medium chain triglyceride[s] having a C_{8-12} fatty acid chain[s]; [synthetic triglycerides; Miglyol 810, Miglyol 812, Miglyol 818, Miglyol 829, Miglyol 840; diglyceride[s]; monoglyceride[s]; monoglyceride and diglyceride free fatty acid[s]; fatty acid ester;] propylene glycol dicaprylate/caprate; linoleic acid ethyl ester; [EPAX6000FA; EPAX4510TG;] a cholesteryl fatty acid ester[s], a C_{12-18} fatty acid monoglyceride[s], a C_{12-18} fatty acid diglyceride[s], and a C_{12-18} fatty acid triglyceride[s] prepared from soybean oil, almond oil, sunflower oil, olive oil, and corn oil with glycerol; a pharmaceutically acceptable monohydric alcohol[s]; a pharmaceutically acceptable alkanol[s]; a pharmaceutically acceptable dihydric alcohol[s]; [glycols;] a pharmaceutically acceptable polyhydroxy compound[s]; glycerin; a pharmaceutically acceptable aromatic ester[s]; benzyl benzoate; diethyl phthalate; propyl gallate; triacetin; diacetin; monoacetin; triethyl citrate; [water soluble organic solvents; propylene carbonate; glycofurol; dimethyl isosorbide; dimethyl isoidide; dimethyl isomannide;] a pharmaceutically suitable hydrophobic organic solvent[s]; a hydrofluorocarbon[s] in the liquid state at ambient temperature and pressure (see page 21); and perflubron.

3. The composition[s] of claim 1 [and 2] where [the non-aqueous carrier system consists of (b)] at least one surfactant component is selected from the group consisting of a natural or synthetic amphiphilic agent[s]; a phospholipid[s]; [cholesterol;] a nonionic surfactant[s]; a polyoxyethylene fatty alcohol ether[s]; a sorbitan fatty acid ester[s]; a polyoxyethylene sorbitan fatty acid ester[s]; [Tweens; sorbitan esters; Myrj glycerol esters;] glycerol triacetate; triacetin; a polyethylene glycol[s]; cetyl alcohol; cetostearyl alcohol; stearyl alcohol; a poloxamer[s]; a polaxamine[s]; a polyoxethylene castor oil derivative[s]; [Cremophors;] vitamin E; D-alpha-tocopheryl polyethylene glycol 1000

succinate; vitamin E TPGS; a PEG glyceryl fatty acid ester[s]; PEG-8 glyceryl caprylate/caprate; [Labrasol;] PEG-4 glyceryl caprylate/caprate; [Labrafac Hydro WL 1219;] PEG-32 glyceryl laurate; [Gelucire 44/14;] PEG-6 glyceryl mono oleate; [Labrafil M 1944 CS;] PEG-6 glyceryl linoleate; [Labrafil M 2125 CS;] a propylene glycol mono fatty acid ester[s]; a propylene glycol di-fatty acid ester[s]; propylene glycol laurate; propylene glycol caprylate/caprate; diethylene glycol monoethyl ether; transcutol; a sorbitan fatty acid ester[s]; [Span fatty acid esters; Span 20;] a monoglyceride[s]; an acetylated monoglyceride[s]; glycerol monooleate; glycerol monostearate; a mono-acetylated monoglyceride[s]; a di-acetylated monoglyceride[s]; monoacetin; diacetin; [carbomers]; [Carbopol;] an anionic surfactant[s]; a fatty acid salt[s]; a bile salt[s]; potassium laurate; triethanolamine stearate; sodium lauryl sulfate; an alkyl polyoxyethylene sulfate[s]; sodium alginate; dioctyl sodium sulfosuccinate; sodium carboxymethylcellulose; calcium carboxymethylcellulose; a cationic surfactant[s]; a pharmaceutically acceptable quaternary ammonium compound[s]; benzalkonium chloride; cetyltrimethylammonium bromide; [and] lauryldimethylbenzylammonium chloride; a substituted cellulose derivative[s]; methylcellulose; hydroxycellulose; hydroxy propylcellulose; hydroxy propylmethylcellulose; noncrystalline cellulose; sodium carboxymethyl cellulose; polyethylene glycol; [PEG; PEG 300; PEG 400; PEG 600;] PEG 1000; PEG 1500; and PEG 3400[; Carbowax; Lutrol E; Hodag PEG;].

4. The [C]composition[s] of claim [1 and 2] 3 in which the [surfactant system comprises at least one] phospholipid is selected from the group consisting of a saturated phospholipid[s], an unsaturated phospholipid[s], a synthetic phospholipid[s], a natural phospholipid[s], and a combination[s] thereof.

5. The composition[s] of claim 1 [and 2] where [the non-aqueous carrier system consists of (c)] at least one hydrophilic component is selected from the group

consisting of a low-molecular weight monohydric alcohol[s]; a low-molecular weight polyhydric alcohol[s]; ethanol; a glycol[s]; glycerol; and a mixture[s] thereof.

6. The [C]composition[s] of claim[s] 1 [and 2 further comprising one or more pharmaceutical excipient useful] in a dosage form (see page 17, line 22) for peroral, parenteral, transdermal, inhalation, or ophthalmic administration of [the] said biologically active substance.

7. The [C]composition[s] of [and processes according to] claim[s] 1 [and 2], wherein the biologically active substance is selected from the group consisting of an antihypertensive drug, an anticholinergic drug, a drug for treating a gastro-intestinal disorder, a hormone, an antineoplastic drug, an NSAID, an anti-fungal agent, an anti-viral agent, a cholesterol controlling agent, an immuno-suppressive peptide, and a protein used in the treatment of diabetes.

8. The [C]composition[s] of [and processes according to] claim[s] 1 [and 2], wherein the biologically active substance is selected from the group consisting of nifedipine, ursodiol, budesonide, peclitaxel, camptothecin, a derivative of peclitaxel, a derivative of camptothecin, piroxicam, itraconazole, acyclovir, a derivative of acyclovir, fenofibrate, cyclosporine, insulin, and a derivative of insulin.

9. The composition[s] of claim[s] 1 [and 2] [wherein the concentration of the biologically active substance is sufficient] for use in sustained or controlled delivery of the biologically active substance.

10. The composition[s] of claim 1 [and 2] where the fluid aqueous medium is selected from the group consisting of water, buffered water, phosphate buffered water, phosphate buffered saline, citrate buffered water, acetate buffered water, water buffered with pharmaceutically acceptable pH controlling agents, water containing salts, water containing sodium chloride, water containing pharmaceutically acceptable salts, water containing soluble agents for lyoprotection, water containing soluble agents for cryoprotection, water containing dextrose, water containing mannitol, water containing trehalose, water containing sucrose, water containing sorbitol, water containing pharmaceutically acceptable lyoprotectants, water containing pharmaceutically acceptable cryoprotectants, water containing polyhydroxy-containing compounds, water containing sugars, water containing polyols, and a mixture thereof.

11. The composition[s] of claim 1 [and 2] where the fluid aqueous medium is selected from the group consisting of a biological fluid, blood, plasma, saliva, urine, a protein-containing solution, an aqueous suspension of a protein, lymph fluid, semen, vaginal fluid, lachrymal fluid, nasal fluid, synovial fluid, cerebral fluid, cerebralspinal fluid, amniotic fluid, pancreatic fluid, pulminary fluid, ascites fluid, fluid from a cyst, gastric fluid, intestinal fluid, a fluid removed from a patient, a diluted biological fluid, a concentrated biological fluid, and a mixture of biological fluids from one or more patients.

12. The composition[s] of claim 1 [and 2] where the fluid aqueous medium contains one or more surface active agent.

13. The composition[s] of claim 1 [and 2] contained in a capsule of [selected from the group consisting of a] hard gelatin [capsule], [a] or soft gelatin [capsule], [and a] or starch [capsule], which capsule dissolves in a fluid aqueous medium, and which capsule optionally comprises a pharmaceutically acceptable coating for controlling the release of the biologically active substance from said capsule in said fluid aqueous medium.

14. The composition[s] of claim 1 [and 2] contained in a tablet, which tablet optionally comprises a pharmaceutically acceptable coating for controlling the release of the biologically active substance.

15. A process for preparing a dosage form of a biologically active substance comprising adding to a fluid aqueous medium a composition comprising stable solid (see page 11, line 8) particles of said [surface modified] water-insoluble biologically active substance having a [mean size] volume weighted mean particle size (see page 15, lines 23-24) in the range of 0.01 to 10 micrometers, which particles are dispersed in a non-aqueous carrier system comprised of:

(a) a non-aqueous hydrophobic liquid (see page 17, line 29) [medium] in which [the]said biologically active substance is not soluble or is poorly soluble; and

(b) a surfactant system consisting of at least one surfactant which is soluble in [the]said non-aqueous hydrophobic liquid (see page 17, line 29) [medium], wherein [and] at least a portion of (see page 16, lines 24-45) which surfactant system absorbs to the surface of [the]said particles [biologically active substance]; and

(c) [optionally] a quantity of not more than about 10% of the total weight of said composition of one or more hydrophilic substance that provides a self-dispersing property to said composition[.],

wherein [said composition self-disperse] upon addition of said composition to said fluid (see page 15, line 30) aqueous medium, said composition self-disperses in said fluid aqueous medium (see page 15, line 30) to form a suspension comprising [components of] droplets (see page 16, line 1) of non aqueous hydrophobic liquid (see page 17, line 29) [medium carrier system] containing particles of said surface stabilized water-insoluble biological substance suspended in the oily droplets of the dispersion (see page 23, lines 24-26) and [stable] particles of said water-insoluble biologically active substance migrated into said fluid aqueous medium (see page 16, line 9) wherein said particles have a size in the range of 0.01 to 10 micrometers and have associated therewith on the surface at least a portion of said surfactant system.

16. The process of claim 15 where at least one component of the non-aqueous hydrophobic liquid is selected from the group consisting of an oil derived from animal origin; a vegetable oil; a fish oil; a fish oil free fatty acid; oleic acid; linoleic acid; a poly-unsaturated fatty acid; caprilic/capric triglyceride; caprylic/capric/linoleic triglyceride; a synthetic medium chain triglyceride having a C_{8-12} fatty acid chain; propylene glycol dicaprylate/caprate; linoleic acid ethyl ester; a cholesteryl fatty acid ester, a C_{12-18} fatty acid monoglyceride, a C_{12-18} fatty acid diglyceride, and a C_{12-18} fatty acid triglyceride prepared from soybean oil, almond oil, sunflower oil, olive oil, and corn oil with glycerol; a pharmaceutically acceptable monohydric alcohol; a pharmaceutically acceptable alkanol; a pharmaceutically acceptable dihydric alcohol; a pharmaceutically

acceptable polyhydroxy compound; glycerin; a pharmaceutically acceptable aromatic ester; benzyl benzoate; diethyl phthalate; propyl gallate; triacetin; diacetin; monoacetin; triethyl citrate; a pharmaceutically suitable hydrophobic organic solvent; and a hydrofluorocarbon in the liquid state at ambient temperature and pressure.

17. The process of claim 15 where at least one surfactant component is selected from the group consisting of a natural or synthetic amphiphilic agent; a phospholipid; a nonionic surfactant; a polyoxyethylene fatty alcohol ether; a sorbitan fatty acid ester; a polyoxyethylene sorbitan fatty acid ester; glycerol triacetate; triacetin; a polyethylene glycol; cetyl alcohol; cetostearyl alcohol; stearyl alcohol; a poloxamer; a polaxamine; a polyoxethylene castor oil derivative; vitamin E; D-alpha-tocopheryl polyethylene glycol 1000 succinate; vitamin E TPGS; a PEG glyceryl fatty acid ester; PEG-8 glyceryl caprylate/caprate; PEG-4 glyceryl caprylate/caprate; PEG-32 glyceryl laurate; PEG-6 glyceryl mono oleate; PEG-6 glyceryl linoleate; a propylene glycol mono fatty acid ester; a propylene glycol di-fatty acid ester; propylene glycol laurate; propylene glycol caprylate/caprate; diethylene glycol monoethyl ether; transcutol; a sorbitan fatty acid ester; a monoglyceride; an acetylated monoglyceride; glycerol monooleate; glycerol monostearate; a mono-acetylated monoglyceride; a di-acetylated monoglyceride; monoacetin; diacetin; an anionic surfactant; a fatty acid salt; a bile salt; potassium laurate; triethanolamine stearate; sodium lauryl sulfate; an alkyl polyoxyethylene sulfate; sodium alginate; dioctyl sodium sulfosuccinate; sodium carboxymethylcellulose; calcium carboxymethylcellulose; a cationic surfactant; a pharmaceutically acceptable quaternary ammonium compound; benzalkonium chloride; cetyltrimethylammonium bromide; lauryldimethylbenzylammonium chloride; a substituted cellulose derivative; methylcellulose; hydroxycellulose; hydroxy propylcellulose; hydroxy propylmethylcellulose; noncrystalline cellulose;

sodium carboxymethyl cellulose; polyethylene glycol; PEG 1000; PEG 1500; and PEG 3400.

18. The process of claim 17 in which the phospholipid is selected from the group consisting of a saturated phospholipid, an unsaturated phospholipid, a synthetic phospholipid, a natural phospholipid, and a combination thereof.

19. The process of claim 15 where at least one hydrophilic component is selected from the group consisting of a low-molecular weight monohydric alcohol[s]; a low-molecular weight polyhydric alcohol[s]; ethanol; a glycol[s]; glycerol; and a mixture[s] thereof.

20. The process of claim 15, wherein the biologically active substance is selected from the group consisting of an antihypertensive drug, an anticholinergic drug, a drug for treating a gastro-intestinal disorder, a hormone, an antineoplastic drug, an NSAID, an anti-fungal agent, an anti-viral agent, a cholesterol controlling agent, an immuno-suppressive peptide, and a protein used in the treatment of diabetes.

21. The process of claim 15, wherein the biologically active substance is selected from the group consisting of nifedipine, ursodiol, budesonide, peclitaxel, a derivative of peclitaxel, camptothecin, a derivative of camptothecin, piroxicam, itraconazole, acyclovir, a derivative of acyclovir, cyclosporine, insulin, and a derivative of insulin.

22. The process of claim 15, wherein the fluid aqueous medium is selected from the group consisting of water, buffered water, phosphate buffered water, phosphate buffered saline, citrate buffered water, acetate buffered

water, water buffered with pharmaceutically acceptable pH controlling agents, water containing salts, water containing sodium chloride, water containing pharmaceutically acceptable salts, water containing soluble agents for lyoprotection, water containing soluble agents for cryoprotection, water containing dextrose, water containing mannitol, water containing trehalose, water containing sucrose, water containing sorbitol, water containing pharmaceutically acceptable lyoprotectants, water containing pharmaceutically acceptable cryoprotectants, water containing polyhydroxy-containing compounds, water containing sugars, water containing polyols, and a mixture thereof.

23. The process of claim 15, wherein the fluid aqueous medium is selected from the group consisting of a biological fluid, blood, plasma, saliva, urine, a protein-containing solution, an aqueous suspension of a protein, lymph fluid, semen, vaginal fluid, lachrymal fluid, nasal fluid, synovial fluid, cerebral fluid, cerebralspinal fluid, amniotic fluid, pancreatic fluid, pulminary fluid, ascites fluid, fluid from a cyst, gastric fluid, intestinal fluid, a fluid removed from a patient, a diluted biological fluid, a concentrated biological fluid, and a mixture of biological fluids from one or more patients.